Assessment of Fetal Lung Maturity by Free-Floating Particles in Amniotic Fluid and Biparietal Diameter by Ultrasonography

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Abstract : **The accuracy of Free-floating particles (FFPs) and biparietal diameter (BPD) detected and measured by ultrasonography for assessment of fetal lung maturity were compared with the lecithin/sphingomyelin (L/S ratio) which was used as the gold standard. One hundred pregnant women in the lately third trimester who required amniocentesis for fetal lung maturity testing, from July 1998 to August 1999 at Siriraj Hospital, were included in this study. Ultrasonography was performed to evaluate the presence of FFPs in the amniotic fluid and the BPD was measured. Amniotic fluid for L/S ratio was obtained by amniocentesis. The presence of FFPs had a 58.3% specificity and a 41.7% false positive rate. A BPD value of at least 94 millimeters had 100% specificity and no false positives. When the presence of FFPs and a BPD value of at least 93 millimeters were used in combination, the test gave 100% specificity and no false positives. The presence of FFPs and a BPD value of at least 93 millimeters detected by real time ultrasonography may be used as predictive parameters to indicate fetal lung maturity.**

เรื่องย่อ : **การประเมินหาความสมบูรณ์ของปอดทารกในครรภ์โดยการตรวจลักษณะความขุ่นของน้ำคร่ำร่วมกับการวัดขนาดศีรษะของทารกด้วยคลื่นเสียงความถี่สูง**

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ทำการศึกษาเพื่อหาความถูกต้องแม่นยำของลักษณะความขุ่นของน้ำคร่ำและขนาดของศีรษะทารกจากการตรวจและวัดด้วยคลื่นเสียงความถี่สูงในการประเมินหาความสมบูรณ์ของปอดทารกในครรภ์ เปรียบเทียบกับการวัดสัดส่วนของเลซิธินและสฟิงโกมัยอีลิน กลุ่มตัวอย่างได้แก่สตรีตั้งครรภ์ในปลายไตรมาสที่สาม ที่มีข้อบ่งชี้ในการเจาะน้ำคร่ำทางหน้าท้องเพื่อตรวจหาความสมบูรณ์ของปอดทารกในครรภ์ในโรงพยาบาลศิริราช ระหว่างเดือนกรกฎาคม พ.ศ. 2541 ถึงเดือนสิงหาคม พ.ศ. 2542 จำนวน 100 คน ทำการศึกษาโดยใช้คลื่นเสียง

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ความถี่สูงตรวจลักษณะความขุ่นของน้ำคร่ำและวัดขนาดศีรษะทารก จากนั้นทำการเจาะน้ำคร่ำทางหน้าท้อง แล้วนำน้ำคร่ำที่เจาะได้ไปทดสอบหาสัดส่วนของเลซิธินและสฟิงโกมัยอีลิน แล้วนำผลที่ได้ทั้งหมดมาประเมินความถูกต้องแม่นยำในการตรวจความสมบูรณ์ของปอดทารกในครรภ์ พบว่าการตรวจน้ำคร่ำมีลักษณะขุ่นมีค่าความจำเพาะเพียงร้อยละ 58.3 และผลบวกลวงสูงถึงร้อยละ 41.7 ส่วนการวัดขนาดศีรษะทารกเมื่อมากกว่าหรือเท่ากับ 94 มิลลิเมตร พบว่ามีความจำเพาะร้อยละ 100 และไม่พบมีผลบวกลวง แต่เมื่อนำวิธีการทั้งสองมาใช้ร่วมกัน พบว่าน้ำคร่ำที่มีลักษณะขุ่นร่วมกับขนาดศีรษะทารกที่มากกว่าหรือเท่ากับ 93 มิลลิเมตร จะมีความจำเพาะร้อยละ 100 และไม่พบว่ามีผลบวกลวงเลย การตรวจพบน้ำคร่ำ มีลักษณะความขุ่นร่วมกับขนาดศีรษะทารกที่มากกว่าหรือเท่ากับ 93 มิลลิเมตร จากการตรวจด้วยคลื่นเสียงความถี่สูง สามารถบ่งบอกถึงความสมบูรณ์ของปอดทารกในครรภ์ได้ดี จึงน่าจะใช้เป็นวิธีตรวจหาความสมบูรณ์ของปอดทารกในครรภ์ได้วิธีหนึ่ง

Prematurity is associated with the respiratory distress syndrome (RDS), which is one of the major causes of perinatal mortality and morbidity.[1] The most important cause of RDS is the deficiency of lecithin (L) and sphingomyelin (S), which are components of fetal lung surfactant and can be found in amniotic fluid. An L/S ratio ≥ 2 indicates fetal lung maturity and the incidence of respiratory distress syndrome is less than 2% in these babies.[2-5]

However, amniocentesis is an invasive technique to obtain amniotic fluid for performing an L/S ratio and other tests. It can cause premature labor, premature rupture of membranes, maternal bleeding, fetal trauma or fetal death.[6]

In order to avoid an invasive technique, non-invasive tests have been used to predict fetal lung maturity. Measurement of ultrasonographic parameters, including biparietal diameter (BPD), femur length, abdominal circumference, placental grading and the turbidity of the amniotic fluid are very useful to predict fetal lung maturity. The combination of multiple parameters gives rise to greater accuracy in the prediction of fetal lung maturity, e.g. combining BPD with the turbidity of amniotic fluid.[7,8]

As the gestation increases, the turbidity of amniotic fluid also increases. This results from the accumulation of desquamated fetal cells, lanugo, scalp hairs and vernix caseosa.[9] Fetal movement causes a swirling of particles, giving the appearance of a blizzard.[10] A fetus with a BPD at least 92 mm. has a low incidence of neonatal RDS.[11-13] The aim of this research is to study the accuracy of the BPD measurements and the turbidity of amniotic fluid detected by ultrasonography to predict fetal lung maturity when an L/S ratio ≥ 2 is used as the gold standard, together with a cut-off point for BPD to predict fetal lung maturity.

MATERIALS AND METHODS

One hundred pregnant women in the lately third trimester were studied at Siriraj Hospital from July 1998 to August 1999. They all underwent amniocentesis before termination of pregnancy for various clinical reasons after an ultrasound examination which was performed by an experted sonologist. Amniotic fluid contaminated by either meconium or blood was excluded from this study. Routine measurement of multiple ultrasonographic parameters, including the detection of amniotic fluid for the presence or absence of FFPs was performed. The FFPs assessment was classified into 3 grades as follows: grade 0, no particle could be detected by ultrasound; grade 1, a few coarse particles were found occasionally; grade 2, numerous fine granules or a lot of coarse particles could be seen at any time during scanning. The fetus was observed without any stimulation.

The gold standard comparison of the test, an L/S ratio, was performed to detect fetal lung maturity by a standardized method.[8] A mature L/S ratio was regarded as 2.0 or greater (which is associated with RDS in less than 2%[9,10]) while an

immature L/S ratio was less than 2.0. The sonologist were blind to these results.

General data was analysed by the SPSS/PC+ programme (statistical package for the social science personal computer plus). A mature L/S ratio and the combined measurements of FFPs and BPD were compared by using the Chi-square test with a value of < 0.05 as significant. Sensitivity, specificity, positive and negative predictive values, false positive and negative rate, accuracy and 95% confidence interval (95% CI) were analysed by a two by two table.

RESULTS

One hundred specimens of amniotic fluid were from the pregnant women with mean age of 27.8 $\pm$ 4.8 years (17-40). There were 27 cases of the first pregnancy, 63 of the second pregnancy and 10 cases of the third pregnancy. The clinical reasons for amniocentesis before termination of pregnancy present in the 100 consecutive pregnant women are shown in Table 1.

Table 1. Number of the patients and clinical reasons to perform amniocentesis before termination of pregnancy.

Indication	Number of the patients	%
Previous cesarean section	43	43.0
Diabetes mellitus	16	16.0
Abnormal presentation	13	13.0
Pregnancy induced hypertension	11	11.0
Placenta previa	10	10.0
Intrauterine growth restriction	7	7.0
Total	100	100.0

From the ultrasound scanning 71 patients were found to show the present of FFPs while the another 29 women had FFPs absent. From 64 women with a maure L/S ratio, 56 had FFPs present and 56 of 71 women with FFPs present had a mature L/S ratio (Table 2).

The sensitivity and specificity of FFPs present for fetal lung maturity were 87.5% (95%CI = 76.3-94.1) and 58.3% (95% CI = 40.9-74) respectively. The positive predictive value was 75% (95% CI = 54.8-85.6) and the negative predictive value was 40.3% (95% CI = 29.1-52.5) while the false positive rate was 19.4%.

When the cut-off point of BPD was at least 92 mm., the specificity and false positive rate were 80.6% and 19.4% respectively (Table 3,4). The cut-off point of BPD at least 94 mm. gives the specificity and false positive rate of 100% and 0% respectively (Table 4).

The larger BPD is associated with higher specificity and lower sensitivity, while the smaller BPD is associated with lower specificity and higher sensitivity (Table 4,5,6).

By the use of FFPs and BPD at the cut-off point of 93 mm. or greater, the test to predict fetal lung maturity gives the highest specificity (100%) and no false positive rate (Table 7).

Table 2 . The association between FFPs and L/S ratio results.

		L/S ratio		Total
		Mature (≥2)	Immature (<2)	
FFPs	Present	56	15	71
	Absent	8	21	29
	Total	64	36	100

Table 3. The association between BPD ≥ 92 mm and L/S ratio results.

		L/S ratio		Total
		Mature (≥2)	Immature (<2)	
BPD	≥92 mm.	21	7	28
	<92 mm.	43	29	72
	Total	64	36	100

Table 4. Comparison between the sensitivity, specificity and false positive rate of the difference cut-off point of BPD measuring by ultrasound and L/S ratio results.

Cut-off point of BPD (mm.)	Sensitivity (%)	Specificity (%)	False positive rate (%)
70	100.0	5.6	94.4
75	100.0	8.3	91.7
80	96.9	25.0	75.0
85	89.1	47.2	52.8
90	57.8	66.7	33.3
91	53.1	66.7	33.3
92	32.8	80.6	19.4
93	18.7	97.2	2.8
94	6.2	100.0	0
95	0	100.0	0

Table 5. Comparison between sensitivity, specificity, positive predictive value, negative predictive value, false positive rate and accuracy of BPD ≥ 92, 93, 94 mm. and L/S ratio.

	BPD ≥ 92 mm.		BPD ≥ 93 mm.		BPD ≥ 94 mm.	
	%	95 % CI	%	95% CI	%	95% CI
Sensitivity	32.8	21.9 - 45.8	18.7	10.5 - 30.8	6.2	2.0 - 16.0
Specificity	80.6	63.9 - 91	97.2	88.0 - 100.0	100.0	88.0 - 100.0
Positive predictive value	75.0	54.8 - 85.6	92.3	69.9 - 100.0	100.0	84.0 - 98.0
Negative predictive value	40.3	29.1 - 52.5	40.2	30.7 - 51.9	37.5	28.0 - 48.0
False positive rate	19.4	8.8 - 36.6	2.8	0 - 12.0	0	0 - 12.0
False negative rate	67.2	54.2 - 78.1	81.3	69.2 - 89.5	93.8	84.0 - 98.0
Accuracy	50	39.9 - 60.1	47	37.0 - 57.2	40	30.5 - 50.3

Table 6. The association between FFPs and BPD at the cut-off point ≥ 92 mm. and L/S ratio.

		L/S ratio		Total
		Mature (≥ 2)	Immature (< 2)	
U/S screening FFPs present and BPD ≥ 92 mm.	Positive	21	5	26
	Negative	43	31	74
Total		64	36	100

Table 7. Comparison between sensitivity, specificity, positive predictive value, negative predictive value, false positive rate, false negative rate and accuracy of the measurements of FFPs and BPD by ultrasonography at the cut-off point of ≥ 92, 93 and 94 mm. and L/S ratio results.

	FFPs & BPD ≥ 92 mm.		FFPs & BPD ≥ 93 mm.		FFPs & BPD ≥ 94 mm.	
	%	95 % CI	%	95% CI	%	95% CI
Sensitivity	32.8	21.9 - 45.8	18.8	10.5 - 30.8	6.3	2.0 - 16.0
Specificity	86.1	69.7 - 94.8	100.0	88.0 - 100.0	100.0	88.0 - 100.0
Positive predictive value	80.8	60.0 - 92.7	100.0	69.9 - 100.0	100.0	84.0 - 98.0
Negative predictive value	41.9	30.7 - 53.9	40.9	30.7 - 51.9	37.5	28.0 - 48.0
False positive rate	13.9	5.2 - 30.3	0	0 - 12.0	0	0 - 12.0
False negative rate	67.2	54.2 - 78.1	81.3	69.2 - 89.5	93.8	84.0 - 98.0
Accuracy	52	40.6 - 67.2	48	37.2 - 60.3	40	32.5 - 49.8

DISCUSSION

RDS is the major cause of perinatal mortality and morbidity, therefore many tests have been arised to predict fetal lung maturity. Most tests need amniocentesis, which is an accepted method, to perform amniotic fluid analysis for L/S ratio. However, this procedure takes risk of fetal and maternal morbidity.[2] RDS is rare in a patient with mature L/S ratio (≥ 2) and the mortality rate is only 0.3%.[3,4,14]

Ultrasonography has currently played roles in predicting fetal lung maturity. BPD measurement, placental grading and FFPs present in amniotic fluid by real time ultrasonographic assessments have been correlated with fetal lung maturity.[7,8,12] The combination of FFPs present and BPD measurement is also the method to predict fetal lung maturity. However, the best test should have high specificity and low false positive rate which indicates low risk of neonatal RDS.

From this study, BPD at least 94 mm. is the best cut-off point to predict fetal lung maturity (Table 5). Also from this study, the specificity is 58.3% and false positive rate is 41.7% by the use of only FFPs. Therefore, only FFPs can not be used to predict fetal lung maturity. The specificity is 100% and false positive rate is 0% when cut-off point of the BPD is 94 mm. or greater (Table 5). The high false positive rate could be minimized when the combination of FFPs present and BPD is used to predict fetal lung maturity. The combination of FFPs present and BPD ≥ 93 mm. gives rise to 100% of specificity and 0% of false positive rate and can be used to predict fetal lung maturity.

However, the contaminated amniotic fluid by meconium and blood was excluded from this study because their particles are aliked FFPs.[15-17] Moreover, the value of L/S ratio would be effected from the meconium and blood.

From this study, the use of ultrasonography to detect FFPs and BPD measurement ≥ 93 mm. can be used to predict fetal lung maturity. Moreover, this non-invasive technique can be used in the patient who takes risk of invasive procedures and many unnecessary invasive procedures can be avoided to perform.

Apart from FFPs and BPD, other parameters such as placental grading, head circumference measurement and fetal weight estimation using ultrasonography should also be assessed together in order to increase the accuracy, specificity and sensitivity in determination of fetal maturity.[7,8,12]

CONCLUSION

The present of FFPs and BPD measurement by ultrasonography can be used to assess fetal lung maturity instead of amniocentesis which is an invasive technique. However, more studied of the combination of multiple parameters should be proceeded to improve the specificity, sensitivity and accuracy of the non-invasive tests and the invasive tests should be reduced in the future.

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